

# HEART

## Editorial

### Should percutaneous devices be used to close a patent foramen ovale after cerebral infarction or TIA?

Approximately one third of the population has a patent foramen ovale (PFO); about the same frequency as having brown hair. Can a normal finding be important in the cause of stroke, and should it change management? In particular should we close a normal hole with an artificial device?

The incidence of PFO in patients with cerebral infarction is about 20–30%, which is similar to that in control subjects.<sup>1,2</sup> This has been taken to imply that PFO is coincidental.<sup>2</sup> However, the incidence of PFO is usually higher, about 50–60%,<sup>3</sup> in cryptogenic cerebral infarcts (those associated with normal carotid ultrasonography and haematological analysis in patients with no atrial fibrillation or other clinical evidence of heart disease). Furthermore, PFOs in patients with cryptogenic stroke are larger than in patients with another potential cause for stroke<sup>4</sup> and in control subjects.<sup>5</sup> Finally, the recurrence rate of cryptogenic stroke is higher if a PFO is detected (14% *v* 7% per 100 patient years).<sup>6</sup>

These facts suggest a role for a PFO, but to establish a high likelihood of causation requires finding a source for emboli. Unless venous investigation is conducted immediately, it is difficult to differentiate primary from secondary deep vein thrombosis (DVT). Hanna *et al* found a DVT in 5 of 16 patients with cryptogenic stroke compared with only 1 of 23 patients with a PFO and an additional cause for stroke and only 1 of 35 patients with a PFO but no stroke.<sup>7</sup> Thrombus has also been found in the pelvic veins alone in 5 of 16 patients with cryptogenic stroke.<sup>8</sup> It has also been suggested that a coexistent atrial septal aneurysm may provide a source for emboli as this combination is a significant determinant of first stroke<sup>5</sup> and recurrence.<sup>9,10</sup> These data suggest that a potential (although not necessarily actual) source for emboli could be found in up to two thirds of patients with PFO and cryptogenic stroke.

#### Should finding a PFO change management?

Should we treat the PFO or the thromboembolic potential or both? How often are other factors such as undetected cerebrovascular disease more important? It makes intuitive sense to give up smoking, stop taking oral contraceptives, and adopt conservative measures—for example, calf exercises on plane journeys. Many physicians do not treat further or might advise aspirin after a first cerebral event. However, should we treat with warfarin and if so why not a percutaneous device to avoid the hazards of long term warfarin?

The risk of recurrence after untreated cryptogenic stroke or transient ischaemic attack (TIA) is not certain. Estimates range from approximately 1% to 10% in the first year.<sup>9,11</sup> However, some patients in these studies were prescribed either aspirin or an oral anticoagulant. A recurrence rate of 8% on aspirin, 3% on an oral anticoagulant but 0% on no active treatment has been reported.<sup>9</sup> Recurrence is related to the combination of PFO and atrial septal aneurysm,<sup>9,10</sup> as well as to hypertension<sup>9</sup> and age<sup>12</sup>

suggesting that treatment of the PFO alone may not always be appropriate. Thus the recurrence rate after surgical closure varies from 0%<sup>13</sup> to 20%<sup>14</sup> with the likelihood of recurrence increasing in the elderly,<sup>14</sup> probably because of factors unrelated to either the PFO or thromboembolism. After percutaneous closure the rate of TIA may be as high as 10%<sup>15</sup>; however, no randomised controlled trials of either medical treatment or closure have been published.

In the absence of consensus, let alone adequate evidence, patients have been treated intuitively. Closure of a PFO has been suggested for patients aged under 60 years in whom there is no alternative cause for stroke and the presence of two or more of the following: transeptal passage of > 50 microbubbles; coexistent atrial septal aneurysm; multiple clinical events; multiple infarcts on computed tomography; Valsalva manoeuvre immediately before the event.<sup>12</sup> The treatment, whether surgical closure, aspirin or warfarin, has not been shown to be an independent determinant of the risk of recurrence,<sup>12</sup> but the treatments were not randomised and there was no control arm. A computer analysis concluding that surgical closure should be considered when the risk of recurrence is > 0.8% per year was based on data from only two studies<sup>9,12</sup> neither of which was randomised or controlled.

Surgical closure of PFOs has a low operative mortality in the young and a low long term complication rate<sup>14</sup> but it does require thoracotomy. Percutaneous closure might offer a more convenient alternative, which would avoid the hazards of long term warfarin should this be contemplated based on intuition. However, unlike warfarin, percutaneous devices have an uncertain natural history. In the past, structural failure has occurred, and dislodgement, supra-ventricular tachycardia, infection, and thromboembolism are theoretical or actual risks.<sup>15</sup>

#### Conclusion

The recurrence rate of cryptogenic cerebral infarction or TIA in patients with PFO is not known accurately, but there is reasonable evidence that PFO is genuinely causative in a proportion of patients. Other factors including age and hypertension also affect the rate of recurrence. Randomised trials of no treatment, aspirin, warfarin, and PFO closure are not available, and current management must be based on intuition. It is intuitively reasonable to use oral anticoagulation in patients aged < 60 years with a large PFO (> 50 microcavitations), no other likely cause of stroke, and a recurrence despite aspirin treatment. Alternatively, PFO closure could be considered in patients at high risk of haemorrhagic complications or who do not want to take warfarin, or when recurrence occurs despite adequate anticoagulation. After the initial stroke or TIA, oral anticoagulation or PFO closure could be considered if the PFO is large, if there was a Valsalva manoeuvre immediately before the event, or if there is a high risk of recurrent

DVT. I think that the long term natural history of current percutaneous devices must be observed in clinical trials before they can be recommended as a routine alternative to surgery or warfarin except in unusual individual circumstances—for example, for a patient with frequent TIAs related to an acute DVT.

J CHAMBERS

Senior Lecturer and Honorary Consultant in Cardiology,  
Guy's and St Thomas' Hospitals,  
Lambeth Palace Road, London SE1 7EH, UK

- Vandenbogaerde J, De Blecker J, Decoo D, *et al.* Transoesophageal echo-Doppler in patients suspected of a cardiac source of peripheral emboli. *Eur Heart J* 1992;13:88–94.
- Jones EF, Calafiore P, Donnan GA, *et al.* Evidence that patent foramen ovale is not a risk factor for cerebral ischemia in the elderly. *Am J Cardiol* 1994;74:596–9.
- Cabanes L, Mas JL, Cohen A, *et al.* Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age. *Stroke* 1993;24:1865–72.
- Hausmann D, Mugge A, Daniel WG. Identification of patent foramen ovale permitting paradoxical embolism. *J Am Coll Cardiol* 1995;26:1030–8.
- Van Camp G, Schulze D, Cosyns B, *et al.* Relation between patent foramen ovale and unexplained stroke. *Am J Cardiol* 1993;71:596–8.
- Comess KA, DeRook FA, Beach KW, *et al.* Transesophageal echocardiography and carotid ultrasound in patients with cerebral ischaemia: prevalence of findings and recurrent stroke risk. *J Am Coll Cardiol* 1994;23:1598–603.
- Hanna JP, Jing Ping Sun, Furan AJ, *et al.* Patent foramen ovale and brain infarct—echocardiographic predictors, recurrence and prevention. *Stroke* 1994;25:782–6.
- Cramer SC, Rordorf G, Kaufman JA, *et al.* Clinically occult pelvic-vein thrombosis in cryptogenic stroke. *Lancet* 1998;351:1927–8.
- Mas J-L, Zuber M. Recurrent cerebrovascular events in patients with patent foramen ovale, atrial septal aneurysm, or both and cryptogenic stroke or transient ischaemic attack. *Am Heart J* 1995;130:1083–8.
- Sacco RL, Shi T, Zamanillo MC, *et al.* Predictors of mortality and recurrence after hospitalized cerebral infarction in an urban community. *Neurology* 1994;44:626–34.
- Bogousslavsky J, Garazi S, Jeanrenaud X, *et al.* Stroke recurrence in patients with patent foramen ovale. *Neurology* 1996;46:1301–5.
- Devuyst G, Bogousslavsky J, Ruchat P, *et al.* Prognosis after stroke followed by surgical closure of patent foramen ovale. *Neurology* 1996;47:1162–6.
- Hommas S, Di Tullio MR, Sacco RL, *et al.* Surgical closure of patent foramen ovale in cryptogenic stroke patients. *Stroke* 1997;28:2376–81.
- Bridges ND, Hellenbrand W, Latson L, *et al.* Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. *Circulation* 1992;86:1902–8.
- Nendaz MR, Sarasin FP, Junod AF, *et al.* Preventing stroke recurrence in patients with patent foramen ovale: antithrombotic therapy, foramen closure, or therapeutic abstention? A decision analytic perspective. *Am Heart J* 1998;135:532–41.

## STAMPS IN CARDIOLOGY

### Exercise testing



Exercise testing is seldom seen on postage stamps. The 2 centavos stamp from Cuba was released in 1971 as part of a set of seven celebrating the 10th anniversary of the first manned space flight, and shows cardiopulmonary exercise testing. A similar stamp was issued by Russia in 1980 to mark the 20th anniversary of the Gagarin Cosmonaut Training Centre. The bicycle ergometer stamp was the highest value in a set of three.

M K DAVIES  
A HOLLMAN